Health Canada
Pest Management Regulatory Agency

Santé Canada
Agence de réglementation de la lutte antiparasitaire

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PROPOSED RE-EVALUATION DECISION

Napropamide

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OVERVIEW

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the herbicide napropamide, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use in Canada of products containing napropamide.

An evaluation of available scientific information found that products containing napropamide do not present unacceptable risks to human health or to the environment. As a condition of the continued registration of napropamide uses, new risk-reduction measures must be included on the labels of all products. No additional data are being requested at this time.

This proposal affects all end-use products containing napropamide registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for napropamide and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of napropamide.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information indicated on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

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[1] "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Napropamide, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian regulatory decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a regulatory decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy).

Based on the health and environmental risk assessments published in the 2005 RED, the USEPA concluded that napropamide was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Napropamide?

Napropamide is a herbicide that is used to control weeds in fruit and vegetable crops, field-grown tobacco as well as ornamentals (field-grown, container-grown, ground cover, flower beds, container plantings as well as highway, industrial and foundation plantings). Napropamide is applied using a variety of ground equipment by farm workers and professional applicators. Homeowners can apply napropamide using a shaker can or granular herbicide applicator.

❖ Health Considerations

♦ Can Approved Uses of Napropamide Affect Human Health?

Napropamide is unlikely to affect your health when used according to the revised label directions. Additional risk-reduction measure statements are required on napropamide labels.

People could be exposed to napropamide by consuming food and water, working as a mixer/loader/applicator or by entering treated sites. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to

protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that napropamide was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions were considered to be applicable to the Canadian situation and equivalent risk-reduction measures are required.

♦ Maximum Residue Limits

The *Food and Drugs Act* prohibits the sale of food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Each MRL value defines the maximum concentration in parts per million (ppm) of a pesticide allowed in/on certain foods. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Napropamide is currently registered in Canada for use on apples, grapes, peaches, pears, highbush blueberries, lowbush blueberries, strawberries, apricots, cherries, plums, asparagus, basil, cabbage, broccoli, cauliflower, brussels sprouts, seeded Chinese broccoli, Chinese mustard cabbage, Chinese radish, seeded and transplanted Chinese cabbage (nappa), transplanted kohlrabi, squash, fuzzy squash, garlic, peppers, pumpkin, tomatoes, rutabagas, cranberries, filbert, walnut and caneberries (blackberries, boysenberries, loganberries, raspberries) and could be used in other countries on crops that are imported into Canada. No specific MRLs have been established for napropamide in Canada. Where no specific MRL has been established, a default MRL of 0.1 ppm applies, which means that pesticide residues in a food commodity must not exceed 0.1 ppm. However, changes to this general MRL may be implemented in the future, as indicated in the Discussion Document DIS2006-01, *Revocation of the 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be set.

❖ Environmental Considerations

♦ What Happens When Napropamide Is Introduced Into the Environment?

Napropamide is unlikely to affect non-target organisms when used according to the revised label directions. Additional risk-reduction measures are required on napropamide labels.

Non-target organisms (e.g. birds, mammals, insects, aquatic organisms and terrestrial plants) may be exposed to napropamide in the environment. Environmental risk is assessed by the risk quotient method—the ratio of the estimated environmental concentration to the relevant effects endpoint of concern. The resulting risk quotients are

compared to corresponding levels of concern. A risk quotient less than the level of concern is considered a low risk to non-target organisms, whereas a risk quotient greater than the level of concern indicates some degree of risk.

The USEPA concluded that the reregistration of napropamide was acceptable provided risk-reduction measures to further protect the environment were implemented. These conclusions were considered to be applicable to the Canadian situation, and equivalent risk-reduction measures are currently in place in Canada. Furthermore, the PMRA will require aquatic and terrestrial buffer zones for the dry flowable formulation of napropamide to protect aquatic organisms and terrestrial plants from spray drift.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of napropamide, the PMRA is proposing further risk-reduction measures for product labels.

- **Human Health**
  - To protect mixer/loader/applicators: additional protective equipment
  - To protect workers re-entering treated sites: a restricted-entry interval

- **Environment**
  - To protect non-target sensitive aquatic organisms and terrestrial plants: buffer zones for aquatic and terrestrial habitats

Next Steps

Before making a final re-evaluation decision on napropamide, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

SCIENCE EVALUATION

1.0 Introduction

Napropamide is a broad spectrum, Resistance Management Group 15 herbicide, which acts by disrupting the growth process during germination by preventing root elongation.

Following the re-evaluation announcement for napropamide, the registrant of the technical grade active ingredient in Canada, indicated that they intended to provide continued support for all uses included on the labels of commercial and domestic end-use products.

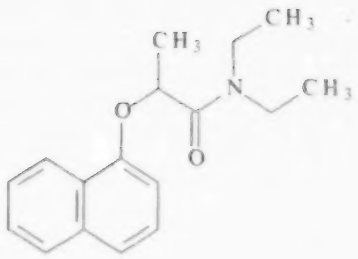
The PMRA used recent assessments of napropamide from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for napropamide, dated September 2005, as well as other information on the regulatory status of napropamide in the United States, can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Napropamide
Function	Herbicide
Chemical family	Alkanamide (acetamide)
Chemical name	
International Union of Pure and Applied Chemistry (IUPAC)	(RS)-*N*,*N*,-diethyl-2-(1-naphthyloxy) propionamide
Chemical Abstracts Service (CAS)	*N*,*N*-diethyl-2-(1-naphthalenyloxy) propanamide
CAS Registry Number	(RS) isomer: 15299-99-7 ®)-(-) isomer: 41643-35-0 (S)-(+) isomer: 41643-36-1
Molecular formula	$C_{17}H_{21}NO_2$

Structural formula



Molecular weight 271.4 amu

One of the raw materials used in the manufacturing process is diethylamine (DEA), which is a nitrosamine precursor. However, nitrosating agents are not used in the process. In addition, the reaction conditions are basic using NaOH in toluene/water and as such, nitrosation of DEA to form *N*-nitrosodiethylamine (NDEA) is not likely.

Therefore, impurities of toxicological concern as identified in Section 2.13.4 of Regulatory Directive DIR98-04, *Chemistry Requirements for the Registration of a Technical Grade of Active Ingredient or an Integrated System Product*, Section 2.13.4 or Toxic Substances Management Policy Track 1 substances as identified in its Regulatory Directive DIR99-03, Appendix II, are not expected to be present or formed in the product.

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	0.053 mPa
Henry's law constant	1.94×10^{-2} Pa m^3 mol^{-1}
UV–visible spectrum	Not expected to absorb UV at $\lambda > 300$ nm
Solubility in water at 25°C	7.4 mg/L
n-Octanol—water partition coefficient	Log K_{ow} = 3.3 (at 25°C)
Dissociation constant (p*K*a)	Not available

2.3 Comparison of Use Patterns in Canada and the United States

Napropamide is a herbicide registered in Canada for the control of annual grasses and broadleaf weeds. It acts by disrupting the growth process during germination by preventing root elongation. It is used in fruit and vegetable crops, field grown tobacco and ornamentals (field-grown, container-grown, ground cover, flower beds, container plantings as well as highway, industrial and foundation plantings). It can be applied either as a granular broadcast treatment, followed by mechanical soil incorporation, or it is formulated as a dry flowable (wettable granules) and is applied using a low pressure boom-type sprayer. One application per

year is made for most crops, with the exception of granular applications to container-grown ornamentals where a second application may be made depending on the conditions. Application of either napropamide formulation may be made at any time of the year to weed free soil; however, the ground should not be frozen, and adequate moisture in the form of rainfall, melting snow or irrigation is required within seven days for a spring or fall application and within two days for a summer application. Typical maximum application rates for napropamide range from 2.25 kg a.i./ha to 4.5 kg a.i./ha for most uses. However, the highest single application rate is 6.7 kg a.i./ha (cranberry and established asparagus).

The American and Canadian use patterns were compared. The Canadian formulation type of end-use products and use sites are among those registered in the United States, with the exception of the following uses: Chinese broccoli, Chinese mustard cabbage, Chinese cabbage (nappa), Chinese radish, kohlrabi, pumpkin, squash, fuzzy squash, basil, rutabaga and garlic. Other uses of napropamide that are registered in the United States, but not in Canada, are grapefruit, lemon, orange, tangerine, tangelo, kiwi fruit, persimmon, avocado, pomegranate, artichoke, fig, mint, olive, eggplant, rhubarb, sweet potato, nectarine, prune, almond, pecan, pistachio and turf (including residential uses).

The maximum Canadian application rates (i.e. 2.25 kg a.i./ha to 4.5 kg a.i./ha for most uses; 6.7 kg a.i./ha for cranberry and established asparagus) are encompassed by the rates assessed in the RED (i.e. 2.25 kg a.i./ha to 4.5 kg a.i./ha for most uses; 6.7 kg a.i./ha for turf and ornamentals; 17 kg a.i./ha for cranberry). The number of applications in Canada are encompassed by the number of applications permitted in the United States (generally one or two applications per year depending on the crop). The Canadian potential application methods are among those registered in the United States. Based on this comparison of use patterns, it was concluded that the USEPA RED for napropamide is an adequate basis for the re-evaluation of Canadian uses of napropamide.

All current Canadian uses are being supported by the registrant and were, therefore, considered in the re-evaluation of napropamide. Appendix I lists all napropamide products that are registered as of 1 April 2007, under the authority of the *Pest Control Products Act*.

3.0 Impact on Human Health and the Environment

In their 2005 RED, the USEPA concluded that the end-use products formulated with napropamide met the safety standard under the American *Food Quality Protection Act* (FQPA) and would not pose unreasonable risks or adverse effects to humans and the environment if used according to the amended labels of all end-use products containing napropamide.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels where no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to napropamide may occur through consumption of food and water, residential exposure, working as a mixer/loader/handler or by entering treated sites. When assessing health risks, the PMRA considers two key factors: the levels where no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required. The toxicological endpoints selected by the USEPA for assessment of risk from occupational exposure are summarized in Appendix II, Table 1.

Workers can be exposed to napropamide through mixing, loading or applying the pesticide and when entering a treated site to conduct activities such as scouting and/or handling of treated crops.

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

The USEPA did not identify a short- or intermediate-term occupational dermal endpoint of concern; therefore, no occupational risk assessment was done for this route of exposure.

Fifteen inhalation exposure scenarios for mixers, loaders, applicators, and other handlers were identified. Among the scenarios assessed in the RED, the following six exposure scenarios were considered relevant to the Canadian situation:

1) mixing/loading dry flowables for groundboom applications;
2) mixing/loading granulars for tractor-drawn spreader applications;
3) applying sprays for groundboom application;
4) applying granulars with a tractor-drawn spreader;
5) applying sprays for high-pressure handwand application; and
6) loading/applying granulars for belly-grinder applications.

Handler exposure analyses were performed using the Pesticide Handlers Exposure Database (PHED) assuming baseline personal protective equipment (PPE) (i.e. long-sleeved shirt, long pants, shoes plus socks, no respirator). Short- and intermediate-term inhalation risk was based on maximum napropamide application rates ranging from 2.2 to 17 kg a.i./ha, an oral no observed adverse effect level (NOAEL) of 30 mg/kg/day from a reproductive toxicity study in the rat and the assumption that the inhalation absorption rate is 100%. Other assumptions included a default female body weight of 60 kg, an 8-hour work day and a daily treatment area of 80 acres/day (≈32 ha/day).

The USEPA reported acceptable short- and intermediate-term inhalation MOEs (i.e. > 100) for all occupational exposure scenarios, ranging from 200 to 33 000. No additional mitigation measures were required with respect to occupational handler exposure. However, baseline PPE was required for all uses, in addition to chemical-resistant gloves. Additional basic hygiene label statements were also recommended.

The RED adequately addressed potential exposure scenarios associated with the Canadian uses of products containing napropamide, and conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires baseline PPE in addition to wearing chemical-resistant gloves during handling to further protect workers. Additional instructions concerning good hygiene practices are also required on labels. The proposed label amendments are listed in Appendix III.

3.1.1.2 Postapplication Exposure and Risk

The USEPA did not assess occupational postapplication risks to agricultural workers because no dermal endpoint of concern was identified. In lieu of a postapplication risk assessment a restricted-entry interval (REI) of 12 hours for all napropamide agricultural use products was required as per the Worker Protection Standard.

This was considered applicable to the Canadian situation, and the PMRA requires a 12-hour REI to further protect workers from postapplication exposure. Proposed label amendments are listed in Appendix III.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach described in Section 3.1.1 above. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix II, Table 1.

Homeowners can be exposed to napropamide through mixing, loading and applying the pesticide and when re-entering a treated site. Toddlers can be exposed via "hand to mouth" and "object to mouth" activities as well as through incidental soil ingestion.

In the United States, napropamide is registered for use, including homeowner use, on lawns and turf or ornamental plants. Risk to adults from handling exposure as well as risk to adults and toddlers from postapplication exposure (including incidental ingestion by toddlers) were assessed. Handler exposure analyses were performed using PHED and the Outdoor Residential Exposure Task Force (ORETF) based on hand or shaker can application of granulars (6.7 kg a.i./unit) or loading/applying granulars using either a belly-grinder or a push-type spreader (3.4 kg a.i./unit). Acceptable adult handler short-term inhalation MOEs ranging from 28 000 and 190 000 were reported (target MOE = 100). Toddler "hand to mouth", "object to

mouth" and "incidental soil ingestion" MOEs were estimated to be 335, 1 340 and 10 000, respectively (target MOE = 100) using the Standard Operating Procedures for Residential Exposure Assessment and based on a maximum application rate of 6.7 kg a.i./ha on turf.

The RED adequately addressed potential exposure scenarios associated with the Canadian residential uses of napropamide (i.e. on ornamentals) and thus conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires no further mitigation measures with respect to residential exposure.

3.1.2.2 Exposure From Food and Drinking Water

No acute endpoints of concern were identified by the USEPA, and napropamide was classified as a Group E carcinogen (no evidence of carcinogenicity). On this basis, no acute or cancer risk assessments were conducted.

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and by comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The ADI is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (Appendix II, Table 1).

An unrefined Tier I chronic dietary risk assessment due to food and drinking water was conducted using Lifeline Model, Version 2.0, which uses food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals from 1994–1996 and 1998, resulting in < 2% of the cPAD for the general American population and all population subgroups, including infants and children. This assessment was based on a cPAD of 0.12 mg a.i./kg bw/day, which was calculated from a chronic rat study (no observed effect level [NOEL] = 12 mg/kg bw/day) and a safety factor of 100-fold. It was assumed that 100% of each commodity was treated and that all residues were at tolerance levels. The estimated maximum chronic drinking water concentration was 4.5 ppb based on Tier I groundwater modelling using Screening Concentration in Ground Water (SCI-GROW). This estimate was based on 10 different crop scenarios modelled with application rates ranging from 1 application of 2.24 kg a.i./ha or 6.7 kg a.i./ha to 2 applications of 4.5 kg a.i./ha. The USEPA considered the estimated combined chronic exposure to napropamide from food and drinking water to be below its level of concern, and no mitigation measure with respect to dietary risk was required.

The current Canadian registered uses of napropamide are encompassed by this assessment, with the exception of the following minor use crops: Chinese radish, fuzzy squash, rutabaga and garlic. Although Chinese broccoli, Chinese mustard cabbage, Chinese cabbage (nappa), kohlrabi, pumpkin, squash and basil were not specifically mentioned as registered uses in the RED, they were included in the assessment. Despite the minor difference in use pattern between the United States and Canada, this assessment is considered to be relevant to Canada because it was a conservative Tier I dietary risk assessment, using tolerance levels and the assumption that 100% of the crop was treated. Furthermore, risk was estimated to be only 2% of the cPAD. The

American tolerances used in the risk assessment were equal to Canadian maximum residue limits (MRLs) (i.e. 0.1 ppm general MRL[3]). The modelled estimated drinking water concentration was based on worst-case scenarios encompassing Canadian application rates. Therefore, the USEPA assessment is considered applicable to the Canadian situation.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to napropamide (i.e. from food, water and residential exposures).

The USEPA estimated a short-term aggregate MOE of 260 (target MOE = 100) for the most highly sensitive subgroup of children 1–2 years old, taking into account food, drinking water and residential exposure. Chronic aggregate risk was estimated to be < 2% of the cPAD for the American population, taking into consideration food and drinking water. Both short-term and chronic aggregate risks were considered to be below the level of concern.

Overall, the Canadian potential aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of napropamide in Canada.

3.1.3 Cumulative Effects

The USEPA has not determined whether napropamide has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that napropamide does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

Napropamide was found to be persistent in the environment and to have the potential to reach surface water via runoff and/or spray drift. Napropamide was not expected to leach into groundwater based on moderate to low mobility in soil.

To assess the ecological risk of napropamide to both terrestrial and aquatic non-target plants and animals, the USEPA calculated risk quotients (RQs) based on appropriate toxicity endpoints and expected environmental concentrations (EECs) and compared the resulting RQs to corresponding levels of concern (LOCs).

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[3] Changes to this general MRL may be implemented in the future, as indicated in Discussion Document DIS2006-01, *Revocation of 0.1 ppm as a General Maximum Residue Limit for Food Pesticide Residues [Regulation B.15.002(1)]*. If and when the general MRL is revoked, a transition strategy will be established to allow permanent MRLs to be promulgated.

Risk assessments for insects and birds were not performed because napropamide was found to be practically non-toxic to honeybees and to be practically non-toxic to birds on an acute oral, subacute dietary and chronic basis. As a result, the potential for napropamide to have adverse effects on pollinators and other beneficial insects was expected to be low, and significant acute and chronic risks to birds were also not expected.

For mammals, EECs were calculated using the Terrestrial Residue Exposure (T-REX) model and based on typical food consumption parameters by various species following application of 1.12 kg a.i./ha to 6.7 kg a.i./ha of napropamide. Acute RQs did not exceed LOCs at any application rate assessed. However, chronic RQs exceeded LOCs (RQs of 1.1 to 21 > LOC of 1.0) at all application rates assessed for mammals feeding on short grass, tall grass and broadleaf plants / small insects and at 6.7 kg a.i./ha for mammals feeding on fruits/pods/large insects. Therefore, the USEPA concluded that there is a chronic risk to mammals from napropamide.

Terrestrial plant EECs were calculated based on application rates ranging from 1.12 kg a.i./ha to 6.7 kg a.i./ha, using the TERRPLANT model that estimates napropamide residues in areas adjacent to the treated field (sheet runoff), wetland areas (channelized runoff) and from spray drift. RQs ranged from 0.1 to 143.8, with RQs of one or more scenarios at each application rate exceeding the plant LOC of 1.0 at all application rates assessed for terrestrial and wetland/riparian plants from sheet and channelized runoff and from spray drift. Therefore, the USEPA concluded that there is a risk to non-target terrestrial and semi-aquatic plants from napropamide.

Aquatic EECs were estimated by taking into account both spray drift and runoff, using the surface water model from the Pesticide Root Zone Model and the Exposure Analysis Modeling System (PRZM/EXAMS). Modelling was based on a variety of scenarios (i.e. different geographical area and crop combinations) assuming both soil incorporation and no soil incorporation, broadcast and banding, single or multiple applications per season and annual application rates ranging from 1.12 kg a.i./ha to 6.7 kg a.i./ha. No acute LOC values were exceeded at any application rate assessed for both freshwater and marine/estuarine fish and invertebrates with the exception of the endangered species LOC (0.05) for acute risk to marine/estuarine invertebrates for some of the scenarios assessed. Chronic LOCs were not exceeded for freshwater fish and invertebrates at all application rates assessed based on limited data.

The plant LOC of 1.0 was not exceeded by any RQ for algae and non-endangered aquatic vascular plants (based on effect concentration at 50% [EC_{50}s] for green algae, blue-green algae and non-endangered aquatic vascular plants) for all application rates assessed. However, endangered species RQs exceeded the plant LOC of 1.0 at all application rates (based on the EC_{50} for endangered aquatic vascular plants).

Based on concerns for acute risks to terrestrial and wetland/riparian non-target plants as well as chronic risks to mammals, the USEPA required a reduction in the total amount of napropamide used in the United States in order to reduce ecological exposure. This reduction in use of napropamide was required via a combination of voluntary cancellations, lowering the use rate of several crops and limiting the number of applications per year for most crops as follows:

- Cancellation of the following uses: pistachio, walnut, grapefruit, lemon, nectarine, orange, tangerine, tangelo, apricot, cherry, peach, plum, prune, apple, pear, fig, avocado, pomegranate, artichoke and olive.

- Limitation of the number of applications permitted to once per year for all remaining uses, with the exception of ornamentals for which two applications will be permitted per year.

- Decrease in the maximum application rate for almonds, pecans, grapes, kiwi fruit and persimmons—8 to 4 lbs per year (≈ 4 to 2 kg per year), cranberries—15 to 9 lbs per year (≈ 7 to 4 kg per year), and turf—6 to 2 lbs per year (≈ 3 to 1 kg per year).

Although conclusions derived from the USEPA RED are considered relevant to the Canadian situation, the required mitigation measures with respect to the environment are not considered applicable in Canada based on the following:

- Canada's use of napropamide equates to approximately one tenth of total napropamide used in the United States. The decrease in application rate for almonds, pecans, kiwi fruit, persimmons and turf are not applicable to Canada since these uses are not registered in Canada. Furthermore, the maximum application rate on grapes (4.5 kg a.i./ha) and cranberries (6.7 kg a.i./ha) on Canadian labels is equal to or lower than the American revised maximum application rates (4.5 kg a.i./ha for grapes and 10 kg a.i./ha for cranberries). In addition, napropamide is typically applied once per season in Canada, with the exception of container-grown ornamentals where two applications per season might be used.

- Because napropamide use and the resulting total environmental load in Canada is about one tenth of that of the United States, use cancellations required in the United States and that are on labels of Canadian end-use products (i.e. apricot, cherry, peach, plum, prune, apple and pear) will not be required in Canada.

- Furthermore, the PMRA will require aquatic and terrestrial buffer zones for the dry flowable formulation of napropamide to protect aquatic organisms and terrestrial plants from spray drift. Proposed label amendments are listed in Appendix III. Inputs to buffer zone models are described in Appendix IV.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy (TSMP), which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances resulting predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the Policy as Track 1 substances.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of napropamide with the following conclusions:

- Napropamide is not bioaccumulative; the *n*-octanol–water partition coefficient (log K_{ow}) is 3.3, which is below the TSMP Track 1 cut-off criterion of ≥ 5.0. Napropamide does not meet all Track 1 criteria; thus, it is not a candidate for Track 1 classification.

- Based on a review of the available chemistry information (see Section 2.1), the technical product is not expected to contain impurities of toxicological concern as identified in DIR98-04 or TSMP Track 1 substances as identified in DIR99-03, Appendix II.

- Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 Proposed Re-evaluation Decision

The PMRA has determined that napropamide is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. Canadian end-use product labels should be amended to include label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. No additional data are being requested at this time.

5.0 Supporting Documentation

PMRA documents, such as DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for napropamide is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

ADI	acceptable daily intake
a.i.	active ingredient
amu	atomic mass unit
ASABE	American Society of Agricultural and Biological Engineers
bw	body weight
CAS	Chemical Abstracts Service
cm	centimetre(s)
cPAD	chronic population adjusted dose
DACO	data code
DEA	diethylamine
EC_{25}	effect concentration at 25%
EC_{50}	effect concentration at 50%
EEC	estimated environmental concentration
EXAMS	Exposure Analysis Modeling System
FIRST	FQPA Index Reservoir Screening Tool
FQPA	*Food Quality Protection Act*
g	gram(s)
h	hour(s)
ha	hectare
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
lb	pound
LOC	level of concern
m	metre(s)
m^3	metre(s) cubed
mg	milligram(s)
mm	millimetre(s)
mm Hg	millimetre mercury
MOE	margin of exposure
MRL	maximum residue limit
N/A	not available
NaOH	sodium hydroxide
NDEA	*N*-nitrosodiethylamine
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEL	no observed effect level
nm	nanometre
ORETF	Outdoor Residential Exposure Task Force
Pa	Pascal
PHED	Pesticide Handlers Exposure Database
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PPE	personal protective equipment
ppb	parts per billion
ppm	parts per million
PRVD	Proposed Re-evaluation Decision
PRZM	Pesticide Root Zone Model
RED	Reregistration Eligibility Decision

REI	restricted-entry interval
RQ	risk quotient
SCI-GROW	Screening Concentration in Ground Water
SF	safety factor
T-REX	Terrestrial Residue Exposure
TSMP	Toxic Substances Management Policy
UF	uncertainty factor
USEPA	United States Environmental Protection Agency
UV	ultraviolet

Appendix I Registered Napropamide Products as of 1 April 2007

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
20122	Technical	United Phosphorus Inc.	Devrinol Technical Herbicide	Solid	94
25297	Commercial	United Phosphorus Inc.	Devrinol 2-G Selective Herbicide Granular	Granular	2
25230	Commercial	United Phosphorus Inc.	Devrinol 10-G Selective Herbicide Granular	Granular	10
25231	Commercial	United Phosphorus Inc.	Devrinol 50 DF Selective Dry Flowable Herbicide	Dry flowable	50
28511	Manufacturing	United Phosphorus Inc.	Devrinol 2-G Manufacturing Concentrate	Granular	2
28512	Domestic	United Phosphorus Inc.	Devrinol 2-G Ready-to-Use Herbicide	Granular	2

Appendix II Toxicological Endpoints for Napropamide Health Risk Assessments

Table 1 Toxicological Endpoints Selected by the USEPA for Napropamide Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study	UF/SF or MOE[a]
Short- and intermediate-term inhalation	Oral NOAEL = 30	Reproductive toxicity study in the rat	100
Chronic dietary	Oral NOAEL = 12	Chronic/ oncogenicity study in the rat	100
	cPAD = 0.12 mg/kg/day (i.e. ADI)		

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments, MOE refers to desired MOE for occupational or residential assessments

Appendix III Label Amendments for Products Containing Napropamide

Canadian end-use product labels must be amended to include the following statements to further protect workers and the environment.

I) For all commercial end-use products containing napropamide, the following statements must be included in a section entitled **PRECAUTIONS**.

Wear long pants, a long-sleeved shirt and chemical-resistant gloves during mixing/loading, clean-up and repair activities.

Do not re-enter or allow re-entry into treated areas until 12 hours after application.

II) For all commercial end-use products containing napropamide, the following statement must be included in a section entitled **DIRECTIONS FOR USE**.

It is recommended that this product not be applied in a way that will contact workers or other persons, either directly or through drift. Only handlers wearing personal protective equipment may be in the area during application.

III) For the commercial dry flowable end-use product, Registration Number 25231, the following statement must be included in a section entitled **DIRECTIONS FOR USE**.

- "Field sprayer application: **DO NOT** apply during periods of dead calm. Avoid application of this product when winds are gusty. **DO NOT** apply with spray droplets smaller than the American Society of Agricultural and Biological Engineers (ASABE) medium classification.

  DO NOT apply by air.

  Buffer zones:

  The buffer zones specified in the table below are required between the point of direct application and the closest downwind edge of sensitive terrestrial habitats (such as grasslands, forested areas, shelter belts, woodlots, hedgerows, rangelands, riparian areas and shrublands), sensitive freshwater habitats (such as lakes, rivers, sloughs, ponds, prairie potholes, creeks, marshes, streams, reservoirs and wetlands) and estuarine/marine habitats.

Method of Application	Crop	Buffer Zones (metres) Required for the Protection of:			
		Aquatic Habitats of Depths:			Terrestrial Habitat
		Less than 1 m	1–3 m	Greater than 3 m	
Field sprayer*	Fuzzy squash	1	0	0	10
	Basil, broccoli, Brussels sprouts, cabbage, cauliflower, Chinese broccoli, Chinese mustard cabbage, Chinese radish, Chinese cabbage, garlic, kohlrhabi, pepper, pumpkin, rutabaga, squash, strawberry, tobacco and tomato	1	0	0	15
	Newly planted fruit trees	2	1	0	25
	Established fruit trees, grapes, caneberries, lowbush and highbush blueberries, asparagus (seedlings and new plantings) and field grown nursery and container stock	2	1	0	30
	Established asparagus	3	1	0	40

* For field sprayer application, buffer zones can be reduced with the use of drift reducing spray shields. When using a spray boom fitted with a full shield (shroud, curtain) that extends to the crop canopy or ground, the labelled buffer zone can be reduced by 70%. When using a spray boom where individual nozzles are fitted with cone-shaped shields that are no more than 30 cm above the crop canopy or ground, the labelled buffer zone can be reduced by 30%.

When a tank mixture is used, consult the labels of the tank-mix partners and observe the largest (most restrictive) buffer zone of the products involved in the tank mixture."

IV) For the commercial dry flowable end-use product, Registration Number 25231, the following statement should be included in a section entitled **ENVIRONMENTAL HAZARDS**.

TOXIC to aquatic organisms and non-target terrestrial plants. Observe buffer zones specified under **DIRECTIONS FOR USE**.

The label amendments presented above do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements, and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

A submission to request label revisions will be required within 90 days of finalization of the re-evaluation decision.

Appendix IV Inputs to Buffer Zone Models

Ground Use Data (from Canadian labels)				
Crop	**Formulation Type**	**Method of Application**	**Number of Application**	**Maximum Application Rate (g a.i./ha)**
Fuzzy squash (transplanted)	Wettable granule	Field sprayer	1	1500
Strawberries	Wettable granule	Field sprayer	1	2000
Basil, rutabagas	Wettable granule	Field sprayer	1	2200
Tomato, pepper, garlic, tobacco, cabbage, broccoli, cauliflower, brussel sprouts, kohlrabi, pumpkin, squash, Chinese broccoli, Chinese cabbage, Chinese mustard cabbage, Chinese radish	Wettable granule	Field sprayer	1	2500
Newly planted fruit trees	Wettable granule	Field sprayer	1	3500
Established fruit trees, grapes, caneberries, lowbush and highbush blueberries, asparagus (seedlings and new plantings) and field grown nursery and container stock	Wettable granule	Field sprayer	1	4500
Established asparagus	Wettable granule	Field sprayer	1	6700

Model Input Data for Aquatic Buffer Zones (from 2005 RED)		
Half-life for aquatic buffer zones	N/A	Assumed stable
Most sensitive freshwater species	*Lemna minor*	1/10 EC_{50} = 0.035 mg a.i./L
Most sensitive estuarine/marine species	Eastern oyster	1/10 EC_{50} = 0.14 mg a.i./L

Model Input Data for Terrestrial Buffer Zones (from 2005 RED)		
Half-life for terrestrial buffer zones	Aerobic soil degradation half-life	446 days
Most sensitive terrestrial plant species EC_{25} for vegetative vigour	*Beta vulgaris*—Vegetative vigour	4 g a.i./ha